VIA MEDICA

BRIEF COMMUNICATION

Cardiology Journal
2019, Vol. 26, No. 6, 793–795
DOI: 10.5603/CJ.2019.0116

ISSN 1897–5593

Is quantitative flow ratio enough to accurately assess intermediate coronary stenosis? A comparison study with fractional flow reserve

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Fractional flow reserve (FFR) is a recommended tool to assess the hemodynamic relevance of borderline stenosis of epicardial coronary arteries but requires costly pressure wires and administration of a hyperemic agent [1]. A novel approach enabling rapid computation of FFR pullbacks from three-dimensional quantitative coronary angiography (3D QCA) has recently been developed [2, 3]. The computational FFR, known as quantitative flow ratio (QFR), may be obtained from 3D QCA using an advanced computer algorithms [2]. However, so far, data on the clinical performance of QFR are rather limited. Thus, the aim herein, was to assess the accuracy of QFR and correlation between QFR and FFR in the assessment of borderline coronary artery stenoses.

Consecutive patients with stable angina, who were scheduled for FFR, were prospectively enrolled. Ethics approval was granted by the institutional ethics review process. Details of FFR procedure were previously described [4, 5]. Computation of QFR was performed offline, using a software package (Medis Suite 2.1.12.2, Medis Medical Imaging System, Leiden, the Netherlands) by two independent corelab analyzers who were blinded to FFR results. The analysis was conducted twice by each analyzer and the mean value (from four calculations) was used for further analysis. The software computed QFR pullback was performed with frame count analysis separately on two diagnostic angiographic projections without pharmacologically induced hyperemia, and empiric hyperemic flow velocities were derived from software computed with two new QFR pullbacks. The QFR pullbacks were chosen based on the best image quality (most well-defined contrast flow) in the frame count analysis as the QFR pullback to compare with the pressure wire-based FFR. The QFR value at the position that matched the location of the pressure transducer on the pressure wire was used for comparison with the FFR value measured by the pressure wire. The flow velocity was derived by dividing the arterial segment length from 3D QCA and the corresponding dye flow time from the frame count analysis. The software allowed for selection of a subsegment of the reconstructed artery with good visualization of the dye flow for calculation of flow velocity. Using the guide catheter for calibration and an edge detection system (CAAS 5.7 QCA system, Pie Medical), the reference vessel diameter and minimum lumen diameter were measured, and the percent diameter stenosis (DS%) was calculated.

A total of 50 patients with 123 borderline coronary artery stenoses were enrolled. Overall, mean age was 66.0 ± 9.3 years, and 72% of patients were male. The left anterior descending artery was the most commonly assessed vessel (39%). Mean angiographic DS% was 44.2 ± 11.7%.

The mean FFR assessed with the femoral vein adenosine infusion at 140 μg/kg/min was 0.82 ± ± 0.10 and 49 (39.8%) vessels had FFR ≤ 0.80, 24 (19.5%) vessels — FFR ≤ 0.75. Figure 1A shows the distribution of the FFR values. Mean QFR value was 0.82 ± 0.09. Forty-seven (38.2%) vessels had QFR value ≤ 0.80 and 30 (24.4%) vessels had QFR ≤ 0.75. A limited intra- and interobserver variability for measuring the QFR was confirmed by intraclass correlation coefficient of 0.991 (95% confidence interval [CI] 0.988–0.993) and 0.990 (95% CI 0.987–0.992), respectively. More importantly, an excellent agreement between FFR and

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Received: 5.11.2019 Accepted: 14.11.2019

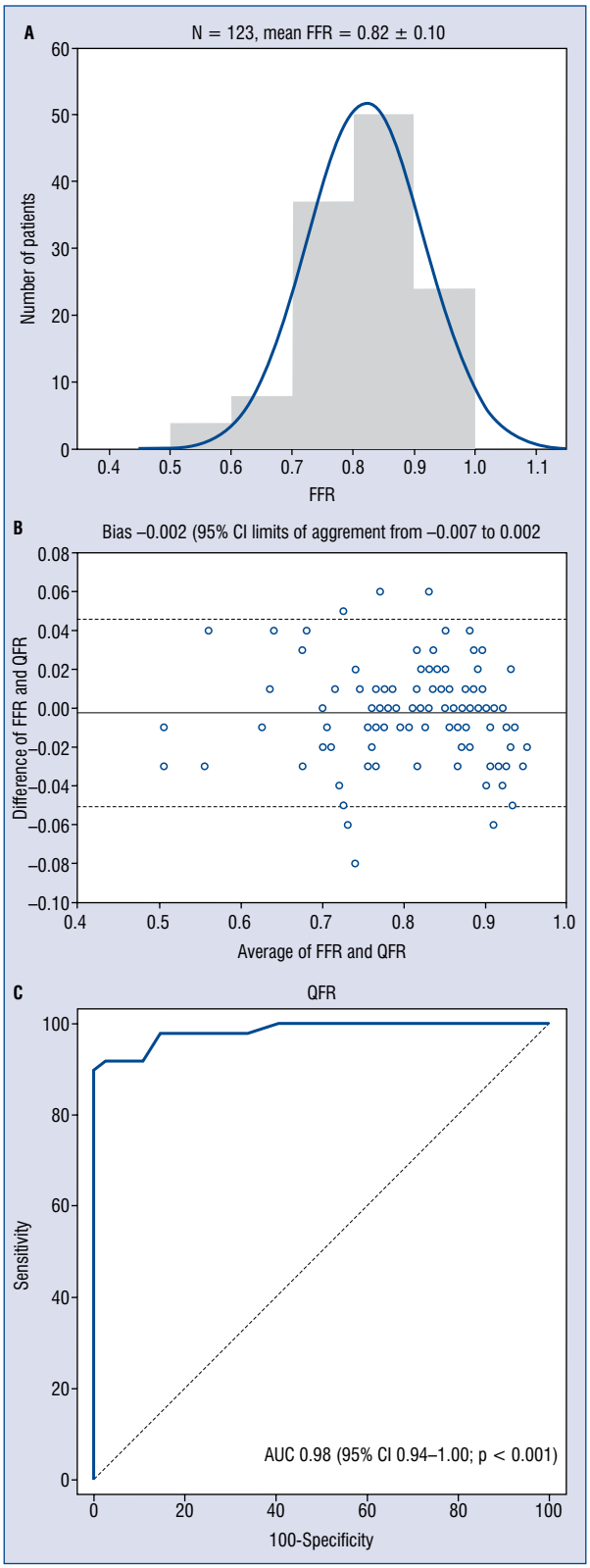

Figure 1. A. Distribution of the fractional flow reserve (FFR) values in the study population; **B.** Overall diagnostic accuracy (AUC in ROC analysis) of quantitative flow ratio (QFR) in detecting FFR ≤ 0.80; **C.** Bland-Altman plot analysis for FFR and QFR.

QFR measurements was confirmed with a mean difference of –0.002 (95% CI –0.007 to 0.002) and ICC 0.965 (95% CI 0.951–0.976) (Fig. 1B). The overall diagnostic accuracy (AUC in ROC analysis) of QFR in detecting FFR ≤ 0.80 was 0.98 (95% CI 0.94–1.00; p < 0.001). The optimal cutoff value for QFR was 0.80 with sensitivity, specificity, and accuracy of 91.8%, 97.3% and 95.1%, respectively. 100.0% sensitivity of QFR was noted for a cutoff value of 0.86, but with relatively low specificity (59.5%) (Fig. 1C). Therefore, QFR values between 0.8 and 0.85 remained in the gray zone and should be verified with conventional invasive FFR measurement.

The results of the current study support the diagnostic value of QFR in assessing the hemodynamic severity of borderline coronary stenosis and yield a promising alternative for non-invasive, drug-free assessment of coronary physiology. QFR was presented by Tu et al. [2] as a novel method for fast computation of FFR from coronary angiography. The major attractiveness of QFR is the avoidance of wiring of the coronary artery and administration of vasodilator drugs, which both are mandatory for FFR assessment. QFR empowered by reliable quantification of vessel dimensions, offers a novel and accurate tool for fast computation of FFR. The processing time is expected to be < 2 min for complete longitudinal FFR computation of each coronary vessel and its major side branches; in other words, FFR of the entire coronary tree would be obtained in < 10 min at the time of angiography [6]. Based on the reported validation against invasive FFR, the high diagnostic accuracy of QFR (88%) relative to the traditional anatomic angiographic measures of minimal lumen area (64%) and DS% (68%) offers better discrimination of the clinical significance of intermediate lesions [2]. The diagnostic accuracy of QFR reported by Tu et al. [6] is very good (88%), with AUC of 0.93, a negative predictive value of 91%, and a positive predictive value of 82% as compared to FFR. In the present study, as well as in the FAVOR studies [7], QFR had similar or even better accuracy in confirmation of hemodynamic significance of borderline coronary stenoses. The QFR assessment may be limited by more obstructive, multivessel or even tandem lesions, and microvascular disease. Another factor contributing to QFR accuracy is its reproducibility when analyzed by different core laboratories. Chang et al. [8] compared QFR results obtained by two independent corelabs interrogating vessels in the FAVOR II study. The mean differ-

ence in contrast-flow QFR between the two core laboratories was 0.004 ± 0.03 (p = 0.040). The mean differences of QFR with respect to FFR were comparable between the two core laboratories. In the current study averaged values of QFR were used obtained by two analysts to reduce the risk of miscalculation.

Acknowledgements

The study was supported by a grant from the Jagiellonian University Medical College (K/ZDS/005469).

Conflict of interest: None declared

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